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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,105	12/20/2001	Carlo Farina	P32331	7825

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EXAMINER

LIU, HONG

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 01/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

### Application No.

10/019,105

### Applicant(s)

FARINA ET AL.

### Examiner

Hong Liu

### Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on 13 November 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-8 and 16-19 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 16-19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Claims 1-8 and 16-19 are pending in this application.

This action is in response to the applicants' amendment and reply filed on November 11, 2003.

### **Response to Arguments**

Applicants' arguments and amendments filed on November 11, 2003 have been fully considered but they are not persuasive. Rejections of Claims 1-8 and 16-19 are maintained.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Claim Rejections - 35 USC § 112***

Claims 6-8 and 16-19 remain rejected under 35 U.S.C. 112, first paragraph for reasons already made of record and notwithstanding applicants' traverse. These method claims remain non-enabled based solely on the over activity of osteoclasts relied on herein. Contrary to what applicants urge is enabled, there is no art-recognized evidence of clinical efficacy for the scope being claimed, and applicants have not provided an adequate traversal to refute the argument made by the examiner. As was previously mentioned in the last office action, Vasikaran's article indicated that inhibitors of osteoclast-mediated bone resorption are only useful in treating Paget's disease of bone, hypercalcaemia and osteolytic bone disease of malignancy, primary and secondary hyperparathyroidism and osteoporosis. Rather than providing evidence to support the argument that the instant compounds are indeed effective in treating all tumors and other diseases as claimed, applicants only generally stated that interpretation of the Vasikaran article is

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“erroneous and contradictory if compared with the commonly accepted teaching derivable from the literature.” Without providing specific evidence, the Examiner will have a difficult time to find the literature that is “erroneous and contradictory” to the Vasikaran article. The language in claim 8 that all the compounds represented by claim 1 can be used to treat tumors is not deemed to be scientifically sound as they are contrary to the current state of art in tumor and cancer treatment. In addition, attorney arguments cannot take the place of evidence on the record which applicants fail to supply (see MPEP 2145 I).

Therefore, in the absence of experimental evidence showing a nexus between osteoclasts antagonism and the effective treatment of all diseases associated with this specific mode of action, the method of treating, let alone preventing (prophylaxis), all diseases apparently contemplated and associated with these antagonists had not been enabled. Note the new utility guidelines stress that tests relied on must be recognized by those skilled in the art as reasonably predicative of in vivo efficacy in man the intended host. Note the remarks made in the recent decision, *Genetech V. Novo Nordisk* 42 USPQ2d 1001 for compliance with 35 U.S.C. 112, par. one., “This specification provides only a starting point, a direction, a direction for further research.” while a different fact situation existed in that case the wording is appropriate herein. Of course the diseases urged supported by applicants are only exemplary and not all inclusive of the scope claimed in these claims.

Rejection #1) is maintained for reasons already made of record. There is no definition of the term in the specification.

Rejection #2) of the previous office action under 35 U.S.C. 112, second paragraph, is maintained for reasons already made of record. The claim language is not limited to one disease

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and there is no clear indication of actual scope from a reading of the specification which describes a variety of disorders/conditions among a list that is nonlimiting. Nothing short of extensive testing would be needed to determine present scope, since the scope could alter over time with more reliable testing becoming available and more diseases being discovered to be affected by tyrosine kinase in ways not yet understood. Such uncertainty in scope does not comply with the second paragraph of 35 U.S.C. 112.

The rejection of the term "substituted and unsubstituted" is maintained for the reasons stated in the previous office. There is no disclosure in the specification what the substituents are.

#### ***Claim Rejections - 35 USC § 102***

All rejections under 35 U.S.C. § 102(a) are maintained. Contrary to applicants' arguments that none of the cited prior art teaches the compounds of formula (I) of claim 1, these references all anticipate the instant claims. For example, when R<sub>1</sub> and R<sub>2</sub> of the instant compound are hydrogen, Y is nitrogen and Z is carbon, R<sub>b</sub> is hydrogen, A is a substituted aryl, R<sub>s</sub> and R<sub>t</sub> are hydrogen, the compound is identical to compound 15 of Barraclough. When Y is carbon and Z is nitrogen and other variables remain the same, the instant compound is a tautomer of compound 4 of Barraclough.

#### ***Claim Rejections - 35 USC § 103***

Rejection under 35 U.S.C. § 103(a) is maintained for the same reason given in the above 102 rejection. There are compounds in the reference that anticipate the instant compounds. Since these compounds are species with the genus of the reference compounds, one of ordinary skill in

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the art would be motivated to select similar compounds from the genus with the expectation that the property of the compounds would remain the same.

***Conclusion***

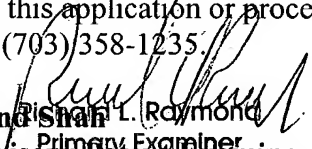
1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to Examiner Hong Liu whose telephone number is (703) 306-5814. The examiner can normally be reached on Monday through Friday from 8:30 AM to 6:00 PM.

If attempts to reach the examiner by the phone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached at (703) 308-4716. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 358-1235.

  
Mukund Shah, L. Raymond  
Supervisory Patent Examiner  
Art Unit 1624

hl  
January 1, 2004